

The EDMVS' Draft Work Plan

Presentation to the EDMVS,
December 10, 2003

Purpose of Today's WorkPlan

- Show progress of EDSP
- Provide the status of each assay
- Project what's next

Tier I Screening Battery

recommended for consideration by EDSTAC

- Steroidogenesis
- Pubertal - female
- Fish Screen
 - aka short term fish reproduction
- Amphibian Metamorphosis
- Estrogen / Androgen receptor binding
- Hershberger
- Uterotrophic

Alternative Assays

recommended for consideration by EDSTAC

Tier I

- Aromatase
- Pubertal male
- Adult 14 –day intact male

Tier ?

- In Utero through Lactation

Tier II Assays

recommended for consideration by EDSTAC

- Mammalian 2-generation
- Avian 2-gen. Reproduction
- Amphibian Development and Repro.
- Invertebrate (Mysid) Lifecycle
- Fish Lifecycle

Tier I Assays

Steroidogenesis

<u>Milestone</u>	<u>Current Status</u>
■ DRP/Protocol -cell based (H295R)	✓ June 02 Dev by ORD
■ Prevalidation -sectional testes optimization -multichem & interlab -cell based (H295R)	✓ June & Aug 03 In Lab In Lab
■ Validation -inter-lab	to lab June 04

Current Status = dates presented to EDMVS &
other information

Pubertals – m&f

<u>Milestone</u>	<u>Current Status</u>
■ DRP equivalent	✓ Dec 01
■ Prevalidation	
-Single Dose Study	✓ Dec 01
-Multi-chemical & multi-dose Protocols	✓ Dec 01
-Multi-chemical & multi-dose -Restricted Feeding Study	Today ✓ July 02
■ Validation (inter-lab)	To lab Feb 04

Fish Screen

Milestones

■ **DRP/Protocol**

■ **Prevalidation**

- **FHM**

- **FHM w/multi-chemicals**

- **Comparative Study Plans:**

-**Results: Comparative Studies**

Vitellogenin Methods, FHM assays

■ **Validation (inter-lab)**

Phase 1A (OECD)

Phase 1B (OECD)

Current Status

✓ **Mar 02**

✓ **Mar 02**

Report writing

✓ **Mar 02**

✓ **Aug 03**
depends on OECD

✓ **Aug 03**

Spring 04

Amphibian Metamorphosis

<u>Milestone</u>	<u>Current Status</u>
■ DRP/Protocol	✓ July 02
■ Pre-validation	
prometamorphosis	
- optimize protocol (US)	Spring 04
- protocol demonstration	to lab
■ Validation (inter-lab OECD)	TBD
-Phase I (protocol optimization)	Spring 04
- "Phase 2" Plan	Spring 04

ER / AR binding

ICCVAM

- | | |
|--|----------------|
| ■ Scientific Expert Panel's retrospective validation | May 2002 |
| ■ EDMVS briefed by ICCVAM | July 2002 |
| ■ Expert Panel Final Report | Sept 2002 |
| ■ ICCVAM Final Report | May 2003 |
| ■ EDSP: AR in lab (preval) | Update Today |
| ■ EDSP: ER in lab (valid) | Oct 02- Oct 04 |

Aromatase

Milestones

■ **DRP / Protocol**

■ **Prevalidation**

-placental microsomal assay ✓ June 03

compare bovine, human,
porcine uterine tissue

-comparison: human placental &
recombinant, multi chem

■ **Validation (inter-lab)**

Current Status

✓ Mar 02

**Today
to lab Jan 04**

In Utero → Lactation

<u>Milestone</u>	<u>Current Status</u>
■ DRP	✓Dec 02
-Protocol review	✓Mar 02
■ Prevalidation	
-Protocol Demo	Data Analysis
-Multi-chem study	TBD
■ Validation (inter-lab)	TBD

Tier II Assays

Mammalian 2-generation

<u>Milestone</u>	<u>Current Status</u>
■ Prevalidation	
One-gen. Ext. Protocol	✓ Dec 02
Propylthiouracil Study	✓ July 02
One-gen Ext. study	✓ June 03
■ Validation (inter-lab)	TBD

Avian 2-gen. Reproduction

<u>Milestone</u>	<u>Current Status</u>
■ DRP/Protocol	✓ Aug 03
■ Prevalidation	
- Avian Dosing Study Plan	✓ Mar 02
- Avian species Comparison	Report writing
-Avian Dose Study	In Lab
-Protocol demo	future
■ Validation (inter-lab OECD)	future

Amphibian Dev. & Repro.

Milestones

Current Status

■ DRP/Protocol

Spring 04

■ Prevalidation

-transferable protocol

future

-multi-chem study

future

■ Validation (inter-lab)

future

Mysid Lifecycle

<u>Milestones</u>	<u>Current Status</u>
■ DRP/Protocol	✓ July 02
■ Prevalidation	
-transferable protocol	Spring 04
-multi-chem study	future
■ Validation (inter-lab OECD)	future

Fish Lifecycle

Milestones

■ DRP/Protocol

■ Prevalidation

-protocol demo

-multi-chem study

■ Validation (inter-lab OECD)

Current Status

✓ Dec 02

In Lab

future

future

Spring/Summer 2004

- Amphibian DRP (Tier II)
- Amphibian Screen protocol (Tier I)
- Fish Screen multi-chemical results
- Fish Screen Phase 1B (OECD)
- Mysid Transferable Protocol
- In Utero Through Lactation
- Avian Species Comparison Results

EPA Docket

www.epa.gov/edocket

June 03 OPPT-2003-0016

August 03 OPPT-2003-0027

Dec 03 OPPT-2003-0064

EDSP website

www.epa.gov/scipoly/oscpendo